

WHAT IS CLAIMED IS:

1. A method for treating a tumor-bearing subject or a precancerous subject, the method comprising administering a therapeutically effective amount of a CD40 binding protein to said subject in conjunction with photodynamic therapy.

2. The method of claim 1 wherein photodynamic therapy includes the steps of administering to the tumor-bearing subject one or more photosensitizers; and exposing the subject to light that is absorbed by the photosensitizer.

3. The method of claim 1 further including the step of administering an active agent selected from the group consisting of:

- a) FasL;
- b) CD30L;
- c) TRAIL; and
- d) TNF alpha

4. The method of claim 1, wherein said CD40 binding protein is selected from the group consisting of:

- (a) an antibody to CD40;
- (b) CD40L;
- (c) soluble CD40L; and
- (d) an oligomeric soluble CD40L fusion protein comprising 1) a soluble CD40L or an antibody to CD40, and 2) a second protein.

5. The method of claim 4, wherein said antibody to CD40 is selected from the group consisting of monoclonal antibody HuCD40-M2 (ATCC HB11459) and antibodies having an antigen binding domain of antibody HuCD40M2.

6. The method of claim 2, wherein said CD40 binding protein is selected from the group consisting of:

- (a) a polypeptide comprising amino acids 1 through 260 of SEQ ID NO:1, 47 through 260 of SEQ ID NO:1, 113 through 260 of SEQ ID NO:1, or 120 through 260 of SEQ ID NO:1;
- (b) a polypeptide comprising amino acids 1 through 261 of SEQ ID NO:2, 47 through 261 of SEQ ID NO:2, 112 through 261 of SEQ ID

NO:2, 113 through 261 of SEQ ID NO:2, or 120 through 261 of SEQ ID NO:2;

(c) a polypeptide comprising a fragment of the polypeptides of SEQ ID NO:1, wherein the fragment binds CD40;

(d) a polypeptide comprising a fragment of the polypeptides of SEQ ID NO:2, wherein the fragment binds CD40;

(e) a polypeptide according to (b) or (c) wherein the cysteine at amino acid 194 of SEQ ID NO:2 is substituted with tryptophan; and

(f) a polypeptide, encoded by the complement of a DNA that hybridizes to a DNA encoding any of the polypeptides of (a)-(e) under conditions of severe stringency (hybridization in 6 X SSC at 63°C overnight; washing in 3 X SSC at 55°C), wherein the encoded polypeptide binds CD40.

7. The method of Claim 4, wherein said second protein is selected from the group consisting of an immunoglobulin Fc domain and an oligomerizing zipper domain.

8. The method of Claim 7, wherein the oligomerizing zipper domain is selected from the group consisting of:

(a) a peptide having an amino acid sequence represented by SEQ ID NO:3; and

(b) a variant of the peptide of (a), wherein the variant consists essentially of the peptide of (a) with one or more conservative amino acid substitutions, wherein the variant is capable of forming an oligomeric CD40L fusion protein.

9. The method of claim 2, wherein the CD40 binding protein comprises amino acids 113 through 261 of SEQ ID NO:2 and the peptide of SEQ ID 3.

10. A method for treating a tumor-bearing subject or a precancerous tumor bearing subject, the method comprising the steps of:

(a) administering a photosensitizer to the subject;

- (b) exposing the subject to light having a wavelength that is absorbed by the photosensitizer; and
- (c) administering a soluble oligomeric CD40L to the subject.

11. The method of claim 10 wherein the soluble oligomeric CD40L comprises amino acids 113-261 of SEQ ID NO:2 and the peptide of SEQ ID NO:3, wherein the cysteine at amino acid 194 of SEQ ID NO:2 is substituted with tryptophan.

12. The method of claim 2, wherein said tumor is selected from the group consisting of a B-lymphoma, a melanoma and a carcinoma.

13. A method for inducing a memory CTL response in a tumor-bearing subject comprising administering a therapeutically effective amount of a CD40 binding protein to said subject in conjunction with photodynamic therapy, wherein the memory CTL response is specific to the tumor.

14. The method of claim 13, wherein said CD40 binding protein is selected from the group consisting of:

- (a) an antibody to CD40;
- (b) CD40L;
- (c) soluble CD40L; and
- (d) an oligomeric soluble CD40L fusion protein comprising 1) a soluble CD40L or an antibody to CD40, and 2) a second protein.

15. The method of claim 13, wherein the CD40 binding protein is selected from the group consisting of:

- (a) polypeptide comprising amino acids 1 through 260 of SEQ ID NO:1, amino acids 47 through 260 of SEQ ID NO:1, amino acids 113 through 260 of SEQ ID NO:1, or amino acids 120 through 260 of SEQ ID NO:1;
- (b) a polypeptide comprising amino acids 1 through 261 of SEQ ID NO:2, amino acids 47 through 261 of SEQ ID NO:2, amino acids 112 through 261 of SEQ ID NO:2, amino acids 113 through 261 of SEQ ID NO:2, or amino acids 120 through 261 of SEQ ID NO:2;
- (c) a polypeptide comprising a fragment of amino acids 47-260 of SEQ ID NO:1, wherein the fragment binds CD40;

(d) a polypeptide comprising a fragment of amino acids 47-261 of SEQ ID NO2, wherein the fragment binds CD40;

(e) a polypeptide of (b) or (d), wherein the cysteine at amino acid 194 is substituted with tryptophan; and

(f) a polypeptide comprising an amino acid sequence that is encoded by the complement of a DNA that hybridizes to a DNA encoding any of the polypeptides of (a)-(f) under conditions of severe stringency (hybridization in 6 X SSC at 63°C overnight; washing in 3 X SSC at 55°C), wherein the encoded polypeptide binds soluble CD40.

16. The method of claim 14, wherein said second protein is selected from the group consisting of an immunoglobulin Fc domain and an oligomerizing zipper domain.

17. The method of Claim 15, wherein the oligomerizing zipper domain selected from the group consisting of:

(a) a polypeptide comprising the amino acids sequence of SEQ ID NO:3; and,

(b) a variant of the peptide of (a), wherein the variant consists essentially of the peptide of (a) with one or more conservative amino acid substitutions, wherein the variant is capable of forming an oligomeric CD40L fusion protein.

18. A method for inducing a memory CTL response in a tumor-bearing subject or a precancerous tumor bearing subject, the method comprising the steps of:

- (a) administering a photosensitizer to the subject;
- (b) exposing the subject to light having a wavelength that is absorbed by the photosensitizer; and
- (c) administering a soluble oligomeric CD40L to the subject.

19. The method of claim 18 wherein the soluble oligomeric CD40L comprises amino acids 113-261 of SEQ ID NO:2 and the peptide of SEQ ID NO:3, wherein the cysteine at amino acid 194 of SEQ ID NO:2 is substituted with tryptophan.

20. A method for treating a tumor-bearing subject comprising the steps of:

- (a) administering to the subject Flt3L in amounts sufficient to mobilize dendritic cells;
- (b) subjecting the subject to PDT by administering a photosensitizer to the subject and exposing the subject to light having a wavelength that is absorbed by the photosensitizer; and
- (d) administering soluble oligomeric CD40L to the subject.

21. The method of claim 20 further including the steps of:

- (a) prior to administering PDT to the subject; obtaining hematopoietic stem or progenitor cells from the subject;
- (b) treating the hematopoietic stem or progenitor cells with Flt3L to obtain dendritic cells; and
- (c) infusing the dendritic cells into the subject.

22. The method of claim 9 further including the steps of:

- (a) prior to administering PDT to the subject, obtaining hematopoietic stem or progenitor cells from the subject;
- (b) treating the hematopoietic stem or progenitor cells with Flt3L to obtain dendritic cells; and
- (c) infusing the dendritic cells into the subject.